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Terms	Documents
L7 and Brij-35	1

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<u>L8</u>	L7 and Brij-35	1	<u>L8</u>
<u>L7</u>	L6 and TRIS	25	<u>L7</u>
<u>L6</u>	L5 and buffer	45	<u>L6</u>
<u>L5</u>	L4 and surfactant	46	<u>L5</u>
<u>L4</u>	L3 and preservative	75	<u>L4</u>
<u>L3</u>	GLP-1	249	<u>L3</u>
<u>L2</u>	6458924.pn.	1	<u>L2</u>
<u>L1</u>	6458924.pn.	1	<u>L1</u>

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1. Document ID: US 6458924 B2

L8: Entry 1 of 1

File: USPT

Oct 1, 2002

US-PAT-NO: 6458924

DOCUMENT-IDENTIFIER: US 6458924 B2

TITLE: Derivatives of GLP-1 analogs

DATE-ISSUED: October 1, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Knudsen; Liselotte Bjerre	Valby			DK
Huusfeldt; Per Olaf	K.o slashed.benhavn K			DK
Nielsen; Per Franklin	V.ae buttet.rl.o slashed.se			DK

US-CL-CURRENT: 530/324; 530/345

Full	Title	CIT.1	REV.1	CLS.1	REF.1	SEQ.1	ATT.1
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L7 and Brij-35

1

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NEWS 8 Sep 16 Experimental properties added to the REGISTRY file
NEWS 9 Sep 16 CA Section Thesaurus available in CAPLUS and CA
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structures available in REGISTRY
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NEWS 32 Apr 17 Polymer searching in REGISTRY enhanced
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NEWS 34 Apr 21 New current-awareness alert (SDI) frequency in
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NEWS 35 Apr 28 RDISCLOSURE now available on STN
NEWS 36 May 05 Pharmacokinetic information and systematic chemical names
added to PHAR
NEWS 37 May 15 MEDLINE file segment of TOXCENTER reloaded
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NEWS 39 May 16 CHEMREACT will be removed from STN

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MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003

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=> s brij-35
L1 905 BRIJ-35

=> s surfactant and use
L2 6877 SURFACTANT AND USE

=> s l1 and l2
L3 32 L1 AND L2

=> s polyoxyethylene
L4 3448 POLYOXYETHYLENE

=> d l3 ti abs ibib 1-10

L3 ANSWER 1 OF 32 MEDLINE
TI Biooxidation of n-hexanol by alcohol oxidase and catalase in biphasic and micellar systems without solvent.
AB Alcohol oxidase from *Pichia pastoris* together with catalase from bovine liver was used to oxidize n-hexanol to hexanal. For this purpose, an aqueous buffer solution was mixed with large amounts of hexanol by simple agitation, yielding a biphasic system, or by adding the nonionic **surfactant Brij 35**. Initial velocities and reaction yields after 24 h were measured as a function of various parameters such as the amounts of enzymes, hexanol, or **surfactant**. High enzymatic activity was determined for hexanol concentrations of between 20 mass% and 80 mass% without using any additional organic solvent. The homogenization of the biphasic systems with the help of **Brij 35** did not yield a significant improvement of the bioconversion, which would justify the **use** of surfactants.

ACCESSION NUMBER: 2002670891 IN-PROCESS
DOCUMENT NUMBER: 22318641 PubMed ID: 12432578
TITLE: Biooxidation of n-hexanol by alcohol oxidase and catalase
in biphasic and micellar systems without solvent.
AUTHOR: Karra-Chaabouni Maha; Pulvin Sylviane; Meziani Abdelghani;
Thomas Daniel; Touraud Didier; Kunz Werner
CORPORATE SOURCE: Laboratoire de Technologie Enzymatique, Universite de
Technologie de Compiègne (UTC), Compiègne, France.
SOURCE: BIOTECHNOLOGY AND BIOENGINEERING, (2003 Jan 5) 81 (1)
27-32.
Journal code: 7502021. ISSN: 0006-3592.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20021115
Last Updated on STN: 20021212

L3 ANSWER 2 OF 32 MEDLINE

TI The mechanisms of rate enhancing and quenching of trichloroethene
photodecay in the presence of sensitizer and hydrogen sources.
AB The reaction mechanisms and rates of trichloroethene (TCE) photodecay in
the presence of photosensitizer (acetone, ACE) and hydrogen sources (
surfactant and triethylamine, TEA) were investigated. Quantum
yields of TCE photodecay in solution with **surfactant**
Brij 35 and optimal ACE dosage are about 25 times higher
than in **Brij 35** alone. However, with an excess ACE
dosage, ACE will act as a light barrier and attenuate the light intensity
available for TCE photodegradation. TCE photodegradation follows a
two-stage kinetics, in which a lag-phase is followed by a fast decay. The
lag-phase distribution depends on initial pH levels and ACE
concentrations. The overall TCE removal was found to be higher at high pH
level, suggesting that free radical reaction is dominant at high pH
levels. The **use** of additional hydrogen source (TEA) in the
reaction can further accelerate the reaction, but overdosing of TEA would
quench the reaction. The possible reaction mechanisms of TCE photodecay
involving ACE and TEA were proposed, and rate-enhancing and rate-quenching
models at low and high TEA concentrations respectively were derived based
on the proposed mechanism, they were found useful for predicting the TEC
decay quantum yields.

ACCESSION NUMBER: 2002403391 MEDLINE
DOCUMENT NUMBER: 22147521 PubMed ID: 12153018
TITLE: The mechanisms of rate enhancing and quenching of
trichloroethene photodecay in the presence of sensitizer
and hydrogen sources.
AUTHOR: Chu W; Choy W K
CORPORATE SOURCE: Department of Civil and Structural Engineering, Research
Centre for Urban Environmental Technology and Management,
The Hong Kong Polytechnic University, Hung Hom, Kowloon..
cewchu@polyu.edu.hk
SOURCE: WATER RESEARCH, (2002 May) 36 (10) 2525-32.
Journal code: 0105072. ISSN: 0043-1354.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20020803
Last Updated on STN: 20030103
Entered Medline: 20030102

L3 ANSWER 3 OF 32 MEDLINE

TI Albumin standards and the measurement of serum albumin with bromocresol

green. 1971.

AB A rapid and reliable method for measuring serum albumin employing bromocresol green is described. The addition of albumin to a solution of bromocresol green in a 0.075 M succinate buffer pH 4.20 results in an increase in absorbance at 628 nm. The absorbance-concentration relationship is linear for samples containing up to 6 g/dl albumin. Bilirubin, moderate lipemia, and salicylate do not interfere with the analysis. The **use** of nonionic **surfactant** (**Brij-35**) reduces the absorbance of the blank, prevents turbidity and provides linearity. The results by this method agree very well with those obtained by electrophoresis and salt fractionation. The method is simple, it has excellent precision and the reagents are stable. A protein standard is introduced which can be employed for both the total serum proteins and albumin determinations.

ACCESSION NUMBER: 97201907 MEDLINE
DOCUMENT NUMBER: 97201907 PubMed ID: 9049440
TITLE: Albumin standards and the measurement of serum albumin with bromocresol green. 1971.
AUTHOR: Dumas B T; Watson W A; Biggs H G
CORPORATE SOURCE: Department of Clinical Pathology, School of Medicine, University of Alabama, Birmingham 35233, USA.
SOURCE: CLINICA CHIMICA ACTA, (1997 Feb 3) 258 (1) 21-30.
Journal code: 1302422. ISSN: 0009-8981.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Biography
Article; (CLASSICAL ARTICLE)
Historical
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; History of Medicine
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970523
Last Updated on STN: 19970523
Entered Medline: 19970509

L3 ANSWER 4 OF 32 MEDLINE
TI **Use** of neutral surfactants for the capillary electrophoretic separation of hydrophobically modified poly(acrylic acids).

AB Hydrophobically modified poly(acrylic acids) (HMPAs) are random copolymers of sodium acrylate and dodecyl acrylamide, containing 0-10% mol/mol of dodecyl grafts. The hydrophobic character of different HMPAs of average molecular weight 150,000 was studied by capillary electrophoresis (CE), using neutral surfactants as buffer additives. The differentiation of the electrophoretic mobilities of HMPAs with their hydrophobicity was achieved through the **use** of nonionic **Brij 35** and zwitterionic DAPS surfactants. A nearly baseline separation of the precursor and three HMPAs derivatives was obtained in a poly(ethylene glycol)-coated capillary with a background electrolyte containing 10 mM N-dodecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate (DAPS) and 10 mM borax (pH 9.2). In addition to CE experiments, the polymer-**surfactant** interactions were also investigated by means of quasi-elastic light scattering (QELS) and viscosimetric measurements. According to the latter results, the separation mechanism was interpreted as an expansion of the polymer coil in the presence of micelles and subsequent change of its frictional properties. A true micellar electrokinetic capillary chromatography (MEKC) partitioning model was discarded on the basis of the relative sizes of the macromolecule and the micelles.

ACCESSION NUMBER: 97008250 MEDLINE
DOCUMENT NUMBER: 97008250 PubMed ID: 8855405
TITLE: **Use** of neutral surfactants for the capillary electrophoretic separation of hydrophobically modified poly(acrylic acids).
AUTHOR: Collet J; Tribet C; Gareil P
CORPORATE SOURCE: Laboratoire d'Electrochimie et de Chimie Analytique, CNRS

URA 216, Ecole Nationale Supérieure de Chimie de Paris,
France.

SOURCE: ELECTROPHORESIS, (1996 Jul) 17 (7) 1202-9.
Journal code: 8204476. ISSN: 0173-0835.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961219

L3 ANSWER 5 OF 32 MEDLINE

TI Anionic-zwitterionic mixed micelles in micellar electrokinetic
chromatography: sodium dodecyl sulfate-N-dodecyl-N,N-dimethylammonium-3-
propane-1-sulfonic acid.

AB A zwitterionic **surfactant**, N-dodecyl-N,N-dimethylammonium-3-
propane-1-sulfonic acid (SB-12), was used in combination with an anionic
surfactant, sodium dodecyl sulfate (SDS), to form a novel
pseudostationary phase for **use** in micellar electrokinetic
chromatography. This mixed micellar system was characterized in terms of
analyte retention, selectivity, efficiency, elution range, and resolution;
and compared to results obtained using only SDS. A typically used SDS
concentration, 20 mM, was chosen as a reference to which comparisons could
be drawn. With 20 mM SDS, the optimum concentration range of 10-20 mM
SB-12 provided efficiencies that were 2-4 times greater than with SDS
alone, with minimal (< 15%) changes in the elution range and
electroosmotic flow. The addition of 40 and 60 mM SB-12 also resulted in
efficiencies on average of 600,000-800,000 theoretical plates/m, but at a
significant reduction in the elution range and peak capacity. Retention
factors (k') for the various neutral analytes increased by 20% with
addition of 10 mM SB-12 and by approximately 60% with addition of 40 and
60 mM SB-12, while operating currents remained constant as SB-12 was
added. Geometrical isomers p-nitrotoluene and m-nitrotoluene, that
co-eluted with 20 mM SDS, were baseline resolved with the addition of 10
mM SB-12; in addition, methylene selectivity was greatest at this
composition. No capillary wall interactions or coating effects were
observed with the SDS-SB-12 mixed micellar system, in contrast to
previously studied anionic-non-ionic mixed micellar system, SDS-
Brij 35. Consequently, migration times were very
repeatable (< or = 1.2% R.S.D.).

ACCESSION NUMBER: 95039794 MEDLINE

DOCUMENT NUMBER: 95039794 PubMed ID: 7952091

TITLE: Anionic-zwitterionic mixed micelles in micellar
electrokinetic chromatography: sodium dodecyl
sulfate-N-dodecyl-N,N-dimethylammonium-3-propane-1-sulfonic
acid.

AUTHOR: Ahuja E S; Preston B P; Foley J P

CORPORATE SOURCE: Department of Chemistry, Villanova University, PA
19085-1699.

SOURCE: JOURNAL OF CHROMATOGRAPHY. B, BIOMEDICAL APPLICATIONS,
(1994 Jul 15) 657 (2) 271-84.
Journal code: 9421796. ISSN: 0378-4347.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199412

ENTRY DATE: Entered STN: 19950110

Last Updated on STN: 19950110

Entered Medline: 19941221

L3 ANSWER 6 OF 32 MEDLINE

TI A retention index for micellar electrokinetic chromatography.
AB A retention index system has been developed for micellar electrokinetic chromatography (MEKC). Three homologous series: alkyl aryl ketones (phenones), 1-nitroalkanes, and alkylbenzenes were studied for **use** as retention index standards. Micellar systems consisting of sodium dodecyl sulfate (SDS), SDS/**Brij 35** (polyoxyethylene lauryl ether), and SDS/SB-12 (N-dodecyl-N, N-dimethylammonium-3-propane-1-sulfonic acid) were used as pseudostationary phases. In addition, three organic modifiers: acetonitrile, methanol, and 1-propanol were used with SDS to evaluate their effect on the retention indices calculated for a set of neutral compounds. Retention indices for the neutral compounds did not vary significantly over the range of **surfactant** concentrations employed for each of the micellar systems (RSD < 2.0% for non-extrapolated retention indices). However, in the systems where an organic modifier was employed, the calculated retention indices showed some variation (RSD < 3.0%) at different SDS concentrations. The 1-nitroalkanes were found to be the most suitable for **use** as retention index standards. Alkyl aryl ketones were found to be effective retention index standards for more hydrophobic solutes, but they were not effective for very hydrophilic solutes even with a large amount of organic modifier added to the operating buffer. The alkylbenzenes were too hydrophobic (highly retained) than the alkyl aryl ketones and, therefore, cannot be recommended for **use** as retention index standards in MEKC.

ACCESSION NUMBER: 94226358 MEDLINE
DOCUMENT NUMBER: 94226358 PubMed ID: 8172368
TITLE: A retention index for micellar electrokinetic chromatography.
AUTHOR: Ahuja E S; Foley J P
CORPORATE SOURCE: Department of Chemistry, Villanova University, PA 19085.
SOURCE: ANALYST, (1994 Feb) 119 (2) 353-60.
Journal code: 0372652. ISSN: 0003-2654.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 19940613
Last Updated on STN: 19940613
Entered Medline: 19940527

L3 ANSWER 7 OF 32 MEDLINE
TI Optimization of selectivity in micellar chromatographic procedures for the determination of drugs in urine by direct injection.
AB Selectivity was optimized for the determination of drugs in urine by direct injection micellar chromatography through changes in specific mobile phase parameters. The role of mobile phase pH and the type of **surfactant** used for mobile phase preparation was investigated. The retention of the urine matrix was found to be minimal between pH 5.5 and 7.5. The non-ionic **surfactant**, polyoxyethylene 23 lauryl ether (**Brij 35**), was found to be the **surfactant** of choice for the separation of drugs from urine. Favourable retention of both the urine background and the analyte was achieved with this **surfactant**. Micellar mobile phases of optimal composition were used to develop chromatographic procedures for the determination of furosemide, hydrochlorothiazide and propranolol in urine. Good accuracy (98-102% of drug recovered), precision (1-4% RSD) and linearity were obtained for all methods. Limits of detection for all drugs were adequate.

ACCESSION NUMBER: 92002379 MEDLINE
DOCUMENT NUMBER: 92002379 PubMed ID: 1911985
TITLE: Optimization of selectivity in micellar chromatographic procedures for the determination of drugs in urine by direct injection.
AUTHOR: Love L J; Fett J J

CORPORATE SOURCE: Department of Chemistry, Seton Hall University, South
Orange, NJ 07079.
SOURCE: JOURNAL OF PHARMACEUTICAL AND BIOMEDICAL ANALYSIS, (1991) 9
(4) 323-33.
Journal code: 8309336. ISSN: 0731-7085.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199111
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19920124
Entered Medline: 19911108

L3 ANSWER 8 OF 32 MEDLINE

TI Novel reagent and method for direct determination of chloride in serum
with a centrifugal analyzer.

AB We report a novel reagent containing ferric perchlorate, perchloric acid,
and polyoxyethylene (23) lauryl ether (**Brij 35**) with
which the concentration of chloride in serum can be measured. We applied
this reagent to **use** with a centrifugal analyzer (CentrifiChem
400) in a dynamic bichromatic procedure, resulting in broad linearity of
the standard curve (0-180 mmol/L), short analysis time (1 min), and little
interference from bilirubin, hemoglobin, turbidity, or bromide ions. The
reagent is simple, contains no mercury, and the combination of low acid
concentration and **surfactant** prevents serum protein
precipitation. Precision is good (for x- = 93 mmol/L, CV = 1.55%), and
results correlate well with those obtained by coulometry (r = 0.974).

ACCESSION NUMBER: 81065198 MEDLINE

DOCUMENT NUMBER: 81065198 PubMed ID: 6254693

TITLE: Novel reagent and method for direct determination of
chloride in serum with a centrifugal analyzer.

AUTHOR: Law W T; Ertingshausen G

SOURCE: CLINICAL CHEMISTRY, (1980 Dec) 26 (13) 1874-7.
Journal code: 9421549. ISSN: 0009-9147.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198102

ENTRY DATE: Entered STN: 19900316

Last Updated on STN: 19900316

Entered Medline: 19810226

L3 ANSWER 9 OF 32 MEDLINE

TI Detergent-containing glucose oxidase reagent for **use** with the
Beckman glucose analyzer.

AB We describe a modified glucose oxidase reagent for **use** in the
polarographic determination of glucose with the Beckman "Glucose
Analyzer." The reagent contains 1 mL/L of a **surfactant** (
Brij-35 250 g/L solution) as the wetting agent instead
of glycerol. Precipitation of components associated with the formulation
recommended by Fischl et al. [Clin. Chem. 21, 760 (1975)] does not occur
with this reagent. It can be used immediately after preparation. When
compared to analytical performance of the commercially prepared reagent,
the precision was unchanged by the modified reagent, but the upper limit
of accurate response was diminished (7.5 g/L vs. 6.7 g/L). The modified
reagent is less expensive than are commercially prepared reagents.

ACCESSION NUMBER: 79105826 MEDLINE

DOCUMENT NUMBER: 79105826 PubMed ID: 761349

TITLE: Detergent-containing glucose oxidase reagent for
use with the Beckman glucose analyzer.

AUTHOR: Bajema L L; Lee W; Zebelman A M; Kenny M A

SOURCE: CLINICAL CHEMISTRY, (1979 Jan) 25 (1) 127-9.

Journal code: 9421549. ISSN: 0009-9147.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197904
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19790425

L3 ANSWER 10 OF 32 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI Biooxidation of n-hexanol by alcohol oxidase and catalase in biphasic and micellar systems without solvent.
AB Alcohol oxidase from *Pichia pastoris* together with catalase from bovine liver was used to oxidize n-hexanol to hexanal. For this purpose, an aqueous buffer solution was mixed with large amounts of hexanol by simple agitation, yielding a biphasic system, or by adding the nonionic **surfactant Brij 35**. Initial velocities and reaction yields after 24 h were measured as a function of various parameters such as the amounts of enzymes, hexanol, or **surfactant**. High enzymatic activity was determined for hexanol concentrations of between 20 mass% and 80 mass% without using any additional organic solvent. The homogenization of the biphasic systems with the help of **Brij 35** did not yield a significant improvement of the bioconversion, which would justify the **use** of surfactants.
ACCESSION NUMBER: 2003:60186 BIOSIS
DOCUMENT NUMBER: PREV200300060186
TITLE: Biooxidation of n-hexanol by alcohol oxidase and catalase in biphasic and micellar systems without solvent.
AUTHOR(S): Karra-Chaabouni, Maha; Pulvin, Sylviane; Meziani, Abdelghani; Thomas, Daniel; Touraud, Didier; Kunz, Werner (1)
CORPORATE SOURCE: (1) Institut fuer Physikalische und Theoretische Chemie, Universitaet Regensburg, D-93040, Regensburg, Germany: werner.kunz@chemie.uni-regensburg.de Germany
SOURCE: Biotechnology and Bioengineering, (January 5 2003) Vol. 81, No. 1, pp. 27-32. print.
ISSN: 0006-3592.
DOCUMENT TYPE: Article
LANGUAGE: English

=> d his

(FILE 'HOME' ENTERED AT 12:13:07 ON 17 MAY 2003)

FILE 'MEDLINE, BIOSIS, DGENE, EMBASE' ENTERED AT 12:13:26 ON 17 MAY 2003

L1 905 S BRIJ-35
L2 6877 S SURFACTANT AND USE
L3 32 S L1 AND L2
L4 3448 S POLYOXYETHYLENE

=> d l3 ti abs ibib 25-32

L3 ANSWER 25 OF 32 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
TI Albumin standards and the measurement of serum albumin with bromcresol green.
AB A rapid and reliable method for measuring serum albumin employing bromcresol green is described. The addition of albumin to a solution of bromcresol green in a 0.075 M succinate buffer pH 4.20 results in an increase in absorbance at 628 nm. The absorbance-concentration relationship is linear for samples containing up to 6 g/dl albumin. Bilirubin, moderate lipemia, and salicylate do not interfere with the analysis. The **use** of a nonionic **surfactant** (

Brij-35) reduces the absorbance of the blank, prevents turbidity and provides linearity. The results by this method agree very well with those obtained by electrophoresis and salt fractionation. The method is simple, it has excellent precision and the reagents are stable. A protein standard is introduced which can be employed for both the total serum proteins and albumin determinations.

ACCESSION NUMBER: 97044258 EMBASE
DOCUMENT NUMBER: 1997044258
TITLE: Albumin standards and the measurement of serum albumin with bromocresol green.
AUTHOR: Doumas B.T.; Watson W.A.; Biggs H.G.
CORPORATE SOURCE: B.T. Doumas, Marquette School of Medicine, Departement of Pathology, 8700 West Wisconsin Avenue, Milwaukee, WI 53226, United States
SOURCE: Clinica Chimica Acta, (1997) 258/1 (21-30).
Refs: 18
ISSN: 0009-8981 CODEN: CCATAR
PUBLISHER IDENT.: S 0009-8981(96)06447-9
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

L3 ANSWER 26 OF 32 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
TI **Use** of neutral surfactants for the capillary electrophoretic separation of hydrophobically modified poly(acrylic acids).
AB Hydrophobically modified poly(acrylic acids) (HMPAs) are random copolymers of sodium acrylate and dodecyl acrylamide, containing 0-10% mol/mol of dodecyl grafts. The hydrophobic character of different HMPAs of average molecular weight 150,000 was studied by capillary electrophoresis (CE), using neutral surfactants as buffer additives. The differentiation of the electrophoretic mobilities of HMPAs with their hydrophobicity was achieved through the **use** of nonionic **Brij 35** and zwitterionic DAPS surfactants. A nearly baseline separation of the precursor and three HMPAs derivatives was obtained in a poly(ethylene glycol)-coated capillary with a background electrolyte containing 10 mM N-dodecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate (DAPS) and 10 mM borax (pH 9.2). In addition to CE experiments, the polymer-**surfactant** interactions were also investigated by means of quasi-elastic light scattering (QELS) and viscosimetric measurements. According to the latter results, the separation mechanism was interpreted as an expansion of the polymer coil in the presence of micelles and subsequent change of its frictional properties. A true micellar electrokinetic capillary chromatography (MEKC) partitioning model was discarded on the basis of the relative sizes of the macromolecule and the micelles.

ACCESSION NUMBER: 96225233 EMBASE
DOCUMENT NUMBER: 1996225233
TITLE: **Use** of neutral surfactants for the capillary electrophoretic separation of hydrophobically modified poly(acrylic acids).
AUTHOR: Collet J.; Tribet C.; Gareil P.
CORPORATE SOURCE: Lab d'Electrochimie/Chimie Anal., CNRS URA 216, Ecole Nationale Sup. de Chimie Paris, 11 rue Pierre et Marie Curie, 75231 Paris Cedex 05, France
SOURCE: Electrophoresis, (1996) 17/7 (1202-1209).
ISSN: 0173-0835 CODEN: ELCTDN
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English

SUMMARY LANGUAGE: English

L3 ANSWER 27 OF 32 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

TI **Use** of micellar media for the fluorimetric determination of ellipticine in aqueous solutions.

AB Ellipticine is a pyridocarbazole alkaloid with interesting antitumour activity. **Use** of neutral ellipticine is hampered by its very low water solubility and therefore this compound has been administered as a salt; however, nitrogen quaternization modifies the antitumour properties of ellipticine. Potential alternatives to quaternization include the **use** of cyclodextrins, and also the **use** of micellar media. The latter possibility is explored in this work as an analytical tool. The results obtained with model anionic (SDS), cationic (CTAB) and neutral (**Brij-35**) surfactants are described. Fluorimetric analysis shows that ellipticine solubilizes completely in the presence of all these compounds, as a result of its aromatic, planar structure. The **use** of micellar media considerably increases the slopes of the calibration curves with improved correlation coefficients (e.g. 0.8904 in water and 0.9982 with SDS). Micellar media also modify proton transfer processes, as a consequence of the apolar environment of the micellar phase. Deprotonation of ellipticine is hampered in SDS because of the relationship between this process and the surface charge of the micelles. Finally, fluorescence quenching in micellar media has been studied, it being found that surfactants provide protection towards this phenomenon.

ACCESSION NUMBER: 96213319 EMBASE

DOCUMENT NUMBER: 1996213319

TITLE: **Use** of micellar media for the fluorimetric determination of ellipticine in aqueous solutions.

AUTHOR: Sbail M.; Lyazidi S.A.; Lerner D.A.; Del Castillo B.; Martin M.A.

CORPORATE SOURCE: Sec. Dept. de Quimica Analitica, Facultad de Farmacia, Universidad Complutense, 28040 Madrid, Spain

SOURCE: Journal of Pharmaceutical and Biomedical Analysis, (1996) 14/8-10 (959-965).

ISSN: 0731-7085 CODEN: JPBADA

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

L3 ANSWER 28 OF 32 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

TI Capillary electrophoresis of seed albumins from Vicia species using uncoated and surface-modified fused silica capillaries.

AB Capillary zone electrophoresis has been developed for the separation of seed albumins from Vicia faba using both uncoated and polyoxyethylene ether (**Brij-35**) coated octadecylsilane derivatized capillaries. Optimal separation conditions were found by studying the effect of pH, buffer composition and applied voltage. The nonionic **surfactant**/C18 coated capillary significantly reduced albumin adsorption and electroosmotic flow (EOF). A gradual washing out of the **surfactant** from the coated capillary during **use** altered not only the magnitude of the EOF, but also its reproducibility. The introduction of hydrophilic polymer solutions between analyses for dynamic modification of the Brij/C18 coated capillary surface prevented desorption of coating material, allowed optimization of resolution and ensured stability of the EOF, CE with surface-modified capillaries was then used to compare seed albumin profiles of several Vicia species. This technique appears to provide a powerful tool for **use** in taxonomic investigations.

ACCESSION NUMBER: 95252145 EMBASE

DOCUMENT NUMBER: 1995252145

TITLE: Capillary electrophoresis of seed albumins from Vicia species using uncoated and surface-modified fused silica capillaries.
AUTHOR: Salmanowicz B.P.
CORPORATE SOURCE: Institute of Plant Genetics, Polish Academy of Sciences, 60-479 Poznan, Poland
SOURCE: Chromatographia, (1995) 41/1-2 (99-106).
ISSN: 0009-5893 CODEN: CHRGB7
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L3 ANSWER 29 OF 32 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

TI Anionic-zwitterionic mixed micelles in micellar electrokinetic chromatography: Sodium dodecyl sulfate-N-dodecyl-N,N-dimethylammonium-3-propane-1-sulfonic acid.

AB A zwitterionic **surfactant**, N-dodecyl-N,N-dimethylammonium-3-propane-1-sulfonic acid (SB-12), was used in combination with an anionic **surfactant**, sodium dodecyl sulfate (SDS), to form a never pseudostationary phase for use in micellar electrokinetic chromatography. This mixed micellar system was characterized in terms of analyte retention, selectivity, efficiency, elution range, and resolution; and compared to results obtained using only SDS. A typically used SDS concentration, 20 mM, was chosen as a reference to which comparisons could be drawn. With 20 mM SDS, the optimum concentration range of 10-20 mM SB-12 provided efficiencies that were 2-4 times greater than with SDS alone, with minimal (<15%) changes in the elution range and electroosmotic flow. The addition of 40 and 60 mM SB-12 also resulted in efficiencies on average of 600,000-800,000 theoretical plates/m, but at a significant reduction in the elution range and peak capacity. Retention factors (k') for the various neutral analytes increased by 20% with addition of 10 mM SB-12 and by approximately 60% with addition of 40 and 60 mM SB-12, while operating currents remained constant as SB-12 was added. Geometrical isomers p-nitrotoluene and m-nitrotoluene, that co-eluted with 20 mM SDS, were baseline resolved with the addition of 10 mM SB-12; in addition, methylene selectivity was greatest at this composition. No capillary wall interactions or coating effects were observed with the SDS-SB-12 mixed micellar system, in contrast to previously studied anionic-non-ionic mixed micellar system, SDS-Brij 35. Consequently, migration times were very repeatable (1.2% R.S.D.).

ACCESSION NUMBER: 94241040 EMBASE

DOCUMENT NUMBER: 1994241040

TITLE: Anionic-zwitterionic mixed micelles in micellar electrokinetic chromatography: Sodium dodecyl sulfate-N-dodecyl-N,N-dimethylammonium-3-propane-1-sulfonic acid.

AUTHOR: Ahuja E.S.; Preston B.P.; Foley J.P.

CORPORATE SOURCE: Department of Chemistry, Villanova University, Villanova, PA 19085-1699, United States

SOURCE: Journal of Chromatography B: Biomedical Applications, (1994) 657/2 (271-284).

ISSN: 0378-4347 CODEN: JCBBEF

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

L3 ANSWER 30 OF 32 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

TI Capillary electrophoresis of some tetracycline antibiotics.

AB Data on the separation of tetracycline antibiotics by capillary electrophoresis are rather limited and have not been reported for micellar

electrokinetic capillary chromatographic separation (MECC). In the present study, the separation of tetracycline, oxytetracycline and chlortetracycline by capillary zone electrophoresis and MECC was investigated. Adding non-ionic surfactants such as Triton X-100 to a 0.2 M phosphate migration buffer of pH 2.2 greatly improved separation. The **use** of mixed micelles enlarged the variety of the micellar phases, e.g. a combination of Tween 20 and Tween 80 provided a similar separation pattern. The addition of .beta.-cyclodextrin to a Triton X-100 and **Brij-35 surfactant** combination did not result in an improved separation. A Triton X-100 and **Brij-35** combination could separate tetracycline and its degradation products 4-epitetracycline (ETC), anhydrotetracycline and 4-epianhydrotetracycline. This enabled us to identify ETC in a commercial tetracycline sample.

ACCESSION NUMBER: 94219666 EMBASE
DOCUMENT NUMBER: 1994219666
TITLE: Capillary electrophoresis of some tetracycline antibiotics.
AUTHOR: Croubels S.; Baeyens W.; Dewaele C.; Van Peteghem C.
CORPORATE SOURCE: Laboratory of Food Analysis, Faculty of Pharmaceutical Sciences, University of Ghent, Harelbekestraat 72,B-9000 Ghent, Belgium
SOURCE: Journal of Chromatography A, (1994) 673/2 (267-274).
ISSN: 0021-9673 CODEN: JCRAEY
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

L3 ANSWER 31 OF 32 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
TI Novel reagent and method for direct determination of chloride in serum with a centrifugal analyzer.
AB We report a novel reagent containing ferric perchlorate, perchloric acid, and polyoxyethylene (23) lauryl ether (**Brij 35**) with which the concentration of chloride in serum can be measured. We applied this reagent to **use** with a centrifugal analyzer (CentrifiChem 400) in a dynamic bichromatic procedure, resulting in broad linearity of the standard curve (0-180 mmol/L), short analysis time (1 min), and little interference from bilirubin, hemoglobin, turbidity, or bromide ions. The reagent is simple, contains no mercury, and the combination of low acid concentration and **surfactant** prevents serum protein precipitation. Precision is good (for x- = 93 mmol/L, CV = 1.55%), and results correlate well with those obtained by coulometry (r = 0.974).

ACCESSION NUMBER: 81045696 EMBASE
DOCUMENT NUMBER: 1981045696
TITLE: Novel reagent and method for direct determination of chloride in serum with a centrifugal analyzer.
AUTHOR: Law W.T.; Ertingshausen G.
CORPORATE SOURCE: Med. Prod. Div., Union Carbide Corp., Tuxedo, N.Y. 10987, United States
SOURCE: Clinical Chemistry, (1980) 26/13 (1874-1877).
CODEN: CLCHAU
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L3 ANSWER 32 OF 32 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
TI Detergent-containing glucose oxidase reagent for **use** with the Beckman glucose analyzer.
AB Described is a modified glucose oxidase reagent for **use** in the polarographic determinations of glucose with the Beckman 'Glucose

Analyzer'. The reagent contains 1 mL/L of a **surfactant** (**Brij-35** 250 g/l solution) as the wetting agent instead of glycerol. Precipitation of components associated with the formulation recommended by Fischl et al. Does not occur with this reagent. It can be used immediately after preparation. When compared to analytical performance of the commercially prepared reagent, the precision was unchanged by the modified reagent, but the upper limit of accurate response was diminished. The modified reagent is less expensive than are commercially prepared reagents

ACCESSION NUMBER: 79128513 EMBASE
DOCUMENT NUMBER: 1979128513
TITLE: Detergent-containing glucose oxidase reagent for
use with the Beckman glucose analyzer.
AUTHOR: Bajema L.L.; Lee W.; Zebelman A.M.; Kenny M.A.
CORPORATE SOURCE: Dept. Lab. Med., Univ. Washington, Seattle, Wash. 98195,
United States
SOURCE: Clinical Chemistry, (1979) 25/1 (127-129).
CODEN: CLCHAU
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English

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NEWS 21 Feb 24 METADEX enhancements
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NEWS 30 Apr 11 Display formats in DGENE enhanced
NEWS 31 Apr 14 MEDLINE Reload
NEWS 32 Apr 17 Polymer searching in REGISTRY enhanced
NEWS 33 Apr 21 Indexing from 1947 to 1956 being added to records in CA/CAPLUS
NEWS 34 Apr 21 New current-awareness alert (SDI) frequency in
WPIDS/WPINDEX/WPIX
NEWS 35 Apr 28 RDISCLOSURE now available on STN
NEWS 36 May 05 Pharmacokinetic information and systematic chemical names
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L3 ANSWER 1 OF 5 WPIDS (C) 2003 THOMSON DERWENT
TI New pharmaceutical formulation comprising a **GLP-1**
compound and a buffer useful for treating diabetes type I or II, obesity,
myocardial infarction, gastric ulcer, dyslipidemia, stroke, arrhythmia,
septicemia, functional dyspepsia.
AN 2003-210208 [20] WPIDS
AB WO2003002136 A UPAB: 20030324
NOVELTY - A pharmaceutical formulation comprising a **GLP-1**
compound and a buffer (the **GLP-1** compound is
GLP-1(7-37) or its analogue having an amino acid residue
of the parent peptide with a lipophilic substituent attached optionally
via a spacer), is new.
DETAILED DESCRIPTION - A pharmaceutical formulation comprising a
GLP-1 compound and a buffer (the **GLP-1**

compound is **GLP-1**(7-37) or its analogue having an amino acid residue of the parent peptide with a lipophilic substituent attached optionally via a spacer). The **GLP-1** compound is present in a concentration of 0.1-100 mg/ml, and the formulation has a **pH** of 7.0-10 provided that if an isotonic agent is present and **pH** is 7.4, then mannitol or NaCl is not the isotonic agent.

An INDEPENDENT CLAIM is included for a method for preparing a physically stable pharmaceutical formulation by preparing a formulation containing the **GLP-1** compound, and a buffer and/or water, where the GLP compound is present at a concentration of 0.1-100 mg/ml, and the formulation has a **pH** of 7-10.

ACTIVITY - Antidiabetic; Antilipemic; Anorectic; Cardiant; Anti-ulcer; Antiarrhythmic; Cerebroprotective; Antiinflammatory; Immunosuppressive.

No biological data given.

MECHANISM OF ACTION - Peptide therapy.

USE - The formulation is useful for reducing blood glucose levels, treating diabetes type I or II, obesity, myocardial infarction, gastric ulcer, dyslipidemia, stroke, left ventricular hypertrophy, arrhythmia, septicemia, irritable bowel disease or functional dyspepsia.

Dwg.0/0

ACCESSION NUMBER: 2003-210208 [20] WPIDS
DOC. NO. CPI: C2003-053588
TITLE: New pharmaceutical formulation comprising a **GLP-1** compound and a buffer useful for treating diabetes type I or II, obesity, myocardial infarction, gastric ulcer, dyslipidemia, stroke, arrhythmia, septicemia, functional dyspepsia.
DERWENT CLASS: B04
INVENTOR(S): ENGELUND, D K; FLINK, J M; JENSEN, S B; LARSEN, S M
PATENT ASSIGNEE(S): (NOVO) NOVO NORDISK AS
COUNTRY COUNT: 99
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003002136	A2	20030109	(200320)*	EN	50
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003002136	A2	WO 2002-DK437	20020627

PRIORITY APPLN. INFO: DK 2002-93 20020118; DK 2001-1010
20010628; DK 2001-1011 20010628; DK 2001-1052
20010704; DK 2001-1053 20010704; DK 2002-92
20020118

L3 ANSWER 2 OF 5 WPIDS (C) 2003 THOMSON DERWENT
TI New amidated glucagon-like peptide useful for the treatment of e.g. diabetes.
AN 2002-557607 [59] WPIDS
CR 2002-519754 [55]; 2002-519755 [55]; 2002-557606 [59]
AB WO 200248192 A UPAB: 20021018
NOVELTY - An amidated glucagon-like peptide (**GLP-1**) with the sequence (S1) as given in the specification, is new.

DETAILED DESCRIPTION - An amidated glucagon-like peptide (GLP-1) with the sequence as given in the specification, is new. The peptide comprises a sequence (S1).

His-Xaa(i)-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Xaa(ii)-Gln-Ala-Ala-Lys-Xaa(iii)-Phe-Ile-Xaa(iv)-Trp-Leu-Val-Lys-Gly-Arg-R designated as Val8-GLP-1(7-37)NH₂.

Xaa (i) = Val

Xaa(ii) = Gly;

Xaa(iii) = Glu;

Xaa(iv) = Ala;

R = Gly-NH₂.

INDEPENDENT CLAIMS are included for the following:

(1) crystals (II) of (I);

(2) a pharmaceutical composition (III) comprising (II);

(3) a pharmaceutical solution formulation (IV) comprising (I);

(4) a lyophilized formulation (V) comprising (I); and

(5) modifying (M1) (I) by:

(a) preparing an aqueous solution comprising an amino acid sequence of the naturally occurring human GLP-1 related peptide as given in the specification and designated as GLP-1

(7 - 37)OH;

(b) adding an enzyme (such as citriconic anhydride) that adds protecting groups to the lysine residues in GLP-1(7 - 37)OH to prevent trypsin from cleaving after the lysine residues;

(c) digesting GLP-1(7 - 37)OH with trypsin;

(d) adding a molar excess of glycineamide hydrochloride; and

(e) removing the protecting groups from the lysine residues.

ACTIVITY - Antidiabetic; Anorectic; Antiinflammatory; Cardiant; Cerebroprotective.

HEK-293 Aurora CRM-BLAM cells expressing the human GLP-1 receptor were seeded and the medium was replaced with plasma free medium. On the third day after seeding, 20 micro l of plasma free medium containing different concentrations of Val8-GLP-1

(7-37)NH₂ (I) (test) and Val8-GLP-1(7-37)OH (control)

were added to each well to generate a dose response curve. After 5 hours of incubation with GLP-1 peptide, beta -lactamase

substrate (20 micro l) was added and incubation continued for 1 hour and the fluorescence was determined on a cytofluor. The in vitro activity of (I) relative to the in vitro activity of Val8-GLP-1

(7-37)OH for different samples was found to be 150, 106, 128, 125, 133, 92, and 79% (average 116%).

MECHANISM OF ACTION - None given.

USE - (I), (II), (III) and (IV) are useful in the manufacture of a medicament for the treatment of diabetes, hyperglycemia, obesity, for the reduction of morbidity and mortality associated with myocardial infarction or stroke, for the attenuation of catabolic changes that occur after surgery, in a mammal (preferably human and animal) (claimed). They are also useful for treatment of irritable bowel syndrome.

ADVANTAGE - The amidated peptide has increased stability, both as a formulated compound as well as with respect to the manufacture, and exhibits increased potency compared to the acid form or the truncated amide form of the analog. The peptide has slightly increased in vitro activity compared to Val8-GLP-1(7-37)OH and a reduced tendency to aggregate in solution. The crystal compositions containing the peptide exhibit satisfactory physical stability for at least 14 days in the TCR (undefined) test and at least 28 days in the modified TCR test with respect to agglomeration and clumping. The peptide is observed to be maintained in a predominant alpha -helix conformation throughout the 14-day test, therefore it can be maximally bioavailable after administration to a mammal. The clinical benefits of the crystal compositions of the peptide are found to be present in the mammal being treated for a prolonged period of time.

Dwg.0/0

ACCESSION NUMBER: 2002-557607 [59] WPIDS

CROSS REFERENCE: 2002-519754 [55]; 2002-519755 [55]; 2002-557606 [59]
 DOC. NO. CPI: C2002-158285
 TITLE: New amidated glucagon-like peptide useful for the treatment of e.g. diabetes.
 DERWENT CLASS: B04 D16
 INVENTOR(S): DIMARCHI, R D; GLAESNER, W; MILLICAN, R L J
 PATENT ASSIGNEE(S): (ELIL) LILLY & CO ELI
 COUNTRY COUNT: 98
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002048192	A2	20020620	(200259)*	EN	50
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2002028608	A	20020624	(200267)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002048192	A2	WO 2001-US43167	20011130
AU 2002028608	A	AU 2002-28608	20011130

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002028608	A Based on	WO 200248192

PRIORITY APPLN. INFO: US 2000-255251P 20001213

L3 ANSWER 3 OF 5 WPIDS (C) 2003 THOMSON DERWENT
 TI Pharmaceutical composition useful in the treatment of e.g. diabetes comprises crystals of peptide, glycine, zinc, alcohol, a buffer and a **preservative**.
 AN 2002-519754 [55] WPIDS
 CR 2002-519755 [55]; 2002-557606 [59]; 2002-557607 [59]
 AB WO 200247715 A UPAB: 20021018
 NOVELTY - A pharmaceutical composition comprises crystals of a peptide having specified sequence as given in the specification, glycine (5 - 100 mM of the peptide), an alcohol (1 - 10% the peptide), zinc (0.5 - 2.5 moles/mole of the peptide), a buffer and a **preservative**.
 DETAILED DESCRIPTION - A pharmaceutical composition of pH 6 - 8.5 comprises:
 (A) crystals of peptide of formula (I);
 (B) glycine at a concentration of 5 - 100 mM;
 (C) an alcohol comprising ethanol or isopropanol at a concentration of 1 - 10 vol.%;
 (D) zinc at a concentration of 0.5 - 2.5 moles/mole of peptide;
 (E) a buffer comprising 2-amino-2-hydroxymethyl-1,3-propanediol (TRIS), maleate or succinate; and
 (F) a **preservative**.
 His-Xaa-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Xaa'-Gln-Ala-Ala-Lys-Xaa''-Phe-Ile-Xaa'''-Trp-Leu-Val-Lys-Gly-Arg-R (I)
 Xaa = Val;
 Xaa' = Gly;
 Xaa'' = Glu;
 Xaa''' = Ala; and
 R = Gly.

INDEPENDENT CLAIMS are also included for:

- (1) Use of the composition in the manufacture of a medicament for treating diabetes, hyperglycemia and obesity in a mammal;
- (2) Preparation of crystals of the peptide (I) involving:
 - (a) preparing a glycine-free solution of the peptide at a pH of 9 - 12;
 - (b) adding glycine (5 - 250 mM);
 - (c) adding the alcohol (2 - 20 vol.%) and zinc (0.2 - 2.5 moles/mole of the peptide);
 - (d) adjusting the solution between pH 7.5 - 10.5; and
 - (e) allowing the crystals of the peptide to form;
- (3) Preparation of the composition including peptide (I) involving:
 - (a) preparing crystals of the peptide;
 - (b) lowering the pH of the crystal suspension formed in the step (3a) to a pH at which at least 97 (preferably at least 98) % of the peptide becomes insoluble,
 - (c) adding a **preservative** and the buffer, and
 - (d) adjusting the pH of the suspension of the step (3c) to 6 - 8.5.

ACTIVITY - Antidiabetic; Anorectic; Antiinflammatory.

MECHANISM OF ACTION - None given.

USE - In the manufacture of a medicament for the treatment of diabetes, hyperglycemia and obesity in a mammal; for treating human or animal by therapy (claimed). For treating irritable bowel syndrome.

ADVANTAGE - The composition exhibits satisfactory and physical stability.

Dwg.0/0

ACCESSION NUMBER: 2002-519754 [55] WPIDS
CROSS REFERENCE: 2002-519755 [55]; 2002-557606 [59]; 2002-557607 [59]
DOC. NO. CPI: C2002-147092
TITLE: Pharmaceutical composition useful in the treatment of e.g. diabetes comprises crystals of peptide, glycine, zinc, alcohol, a buffer and a **preservative**.
DERWENT CLASS: B04
INVENTOR(S): DODD, S W; NG, K; RINELLA, J V J; WATTS, E A
PATENT ASSIGNEE(S): (ELIL) LILLY & CO ELI
COUNTRY COUNT: 98
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 2002047715	A2	20020620	(200255)*	EN	68
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ					
NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK					
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR					
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO					
RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2002033929	A	20020624	(200267)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

WO 2002047715	A2	WO 2001-US43188	20011206
AU 2002033929	A	AU 2002-33929	20011206

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 2002033929	A Based on	WO 200247715

PRIORITY APPLN. INFO: US 2000-255251P 20001213

L3 ANSWER 4 OF 5 WPIDS (C) 2003 THOMSON DERWENT
 TI Shelf-stable pharmaceutical formulation useful for treating diabetes
 comprises **glucagon-like peptide-1**
 molecule, **preservative** and tonicity modifier.
 AN 2000-442534 [38] WPIDS
 AB WO 200037098 A UPAB: 20000811
 NOVELTY - Shelf-stable pharmaceutical formulation (I) comprises
glucagon-like peptide-1 (GLP
-1) molecule, **preservative** and tonicity modifier and
 has a **pH** of 8.2-8.8.
 ACTIVITY - Antidiabetic; hypoglycemic; hyperglycemic.
 MECHANISM OF ACTION - Glucose mediated insulin secretion regulator.
 USE - Useful for enhancing the expression of insulin in a mammalian
 pancreatic beta -type islet, treating diabetes and for providing meal time
 glycemic control and basal glycemic control with a single injection.
 ADVANTAGE - The formulation is shelf-stable (claimed). The
 formulation has increased physical and chemical stability relative to
 conventional peptide formulations.
 Dwg.0/0

ACCESSION NUMBER: 2000-442534 [38] WPIDS
 DOC. NO. CPI: C2000-134655
 TITLE: Shelf-stable pharmaceutical formulation useful for
 treating diabetes comprises **glucagon-**
like peptide-1 molecule,
preservative and tonicity modifier.
 DERWENT CLASS: B04
 INVENTOR(S): BRADER, M L; PEKAR, A H
 PATENT ASSIGNEE(S): (ELIL) LILLY & CO ELI
 COUNTRY COUNT: 91
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000037098	A1	20000629	(200038)	* EN	27
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL					
OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES					
FI GB GD GE HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU					
LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM					
TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000023734	A	20000712	(200048)		
EP 1140148	A1	20011010	(200167)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT					
RO SE SI					
MX 2001005648	A1	20010801	(200238)		
JP 2002532557	W	20021002	(200279)		30

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000037098	A1	WO 1999-US30395	19991221
AU 2000023734	A	AU 2000-23734	19991221
EP 1140148	A1	EP 1999-967463	19991221
		WO 1999-US30395	19991221
MX 2001005648	A1	MX 2001-5648	20010605
JP 2002532557	W	WO 1999-US30395	19991221
		JP 2000-589208	19991221

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 2000023734 A Based on WO 200037098
EP 1140148 A1 Based on WO 200037098
JP 2002532557 W Based on WO 200037098

PRIORITY APPLN. INFO: US 1998-113499P 19981222

L3 ANSWER 5 OF 5 WPIDS (C) 2003 THOMSON DERWENT

TI Aqueous solution of glucagon or **glucagon-like peptide-1** stabilized with charged detergent, for treating diabetes or obesity.

AN 1999-561858 [47] WPIDS

CR 1998-207039 [18]; 1998-239721 [21]; 1999-540500 [45]; 1999-540507 [45];
1999-540561 [45]; 1999-540562 [43]; 1999-550859 [46]; 2000-072123 [06];
2001-595691 [50]

AB WO 9947160 A UPAB: 20020603

NOVELTY - Aqueous solution comprises:

(i) at least 0.1 mg/ml at least one peptide (I), i.e. glucagon or **glucagon-like peptide-1 (GLP-1)**, or their analogs or derivatives and

(ii) at least one detergent (II), other than dodecyl phosphocholine.

(I) has at least two positive or negative charges or at least one charge of each sign.

ACTIVITY - Antidiabetic; anti-obesity.

MECHANISM OF ACTION - Glucagon is involved in glycogenolytic and gluconeogenesis processes (it also has a spasmolytic effect on smooth muscle) while **GLP-1** promotes secretion of insulin and suppresses that of glucagon. The polar head of (II) interacts with charged side chains in (I) while the hydrophobic tail interacts with the hydrophobic patch in (I).

USE - The solution is used (claimed) to treat (non-)insulin-dependent diabetes mellitus and obesity. Glucagon is also used in radiology as a spasmolytic and for treating hypoglycemia.

ADVANTAGE - (II) stabilizes the solutions, which are available for immediate use and can be stored for a long time at 4-25 deg. C. The solutions may have **pH** between 4 and 9, allowing selection of conditions that suppress chemical degradation. (II) are made from natural materials so have better biological compatibility than known detergents.
Dwg.0/7

ACCESSION NUMBER: 1999-561858 [47] WPIDS

CROSS REFERENCE: 1998-207039 [18]; 1998-239721 [21]; 1999-540500 [45];
1999-540507 [45]; 1999-540561 [45]; 1999-540562 [43];
1999-550859 [46]; 2000-072123 [06]; 2001-595691 [50]

DOC. NO. CPI: C1999-163789

TITLE: Aqueous solution of glucagon or **glucagon-like peptide-1** stabilized with charged detergent, for treating diabetes or obesity.

DERWENT CLASS: B04 B05

INVENTOR(S): KAARSHOLM, N C

PATENT ASSIGNEE(S): (NOVO) NOVO-NORDISK AS; (NOVO) NOVO NORDISK AS

COUNTRY COUNT: 85

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
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WO 9947160	A1	19990923	(199947)*	EN	27
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RW:	AT	BE	CH	CY	DE	DK	EA	ES	FI	FR	GB	GH	GM	GR	IE	IT	KE	LS	LU	MC	MW	NL
	OA	PT	SD	SE	SL	SZ	UG	ZW														

W:	AL	AM	AT	AU	AZ	BA	BB	BG	BR	BY	CA	CH	CN	CU	CZ	DE	DK	EE	ES	FI	GB	GD
	GE	GH	GM	HR	HU	ID	IL	IN	IS	JP	KE	KG	KP	KR	KZ	LC	LK	LR	LS	LT	LU	LV
	MD	MG	MK	MN	MW	MX	NO	NZ	PL	PT	RO	RU	SD	SE	SG	SI	SK	SL	TJ	TM	TR	TT
	UA	UG	UZ	VN	YU	ZW																

AU 9926125	A	19991011	(200008)		
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EP 1061947	A1	20001227	(200102)	EN	
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R:	AT	BE	CH	CY	DE	DK	ES	FI	FR	GB	GR	IE	IT	LI	LU	MC	NL	PT	SE
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US 6384016 B1 20020507 (200235)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9947160	A1	WO 1999-DK115	19990308
AU 9926125	A	AU 1999-26125	19990308
EP 1061947	A1	EP 1999-906095	19990308
		WO 1999-DK115	19990308
US 6384016	B1 Provisional	US 1998-78422P	19980318
		US 1999-265141	19990308

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9926125	A Based on	WO 9947160
EP 1061947	A1 Based on	WO 9947160

PRIORITY APPLN. INFO: US 1998-78422P 19980318; EP 1998-610006
19980313

=> file uspatful
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
22.81	23.02

FULL ESTIMATED COST

FILE 'USPATFULL' ENTERED AT 13:22:18 ON 15 MAY 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 15 May 2003 (20030515/PD)
FILE LAST UPDATED: 15 May 2003 (20030515/ED)
HIGHEST GRANTED PATENT NUMBER: US6564383
HIGHEST APPLICATION PUBLICATION NUMBER: US2003093849
CA INDEXING IS CURRENT THROUGH 15 May 2003 (20030515/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 15 May 2003 (20030515/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2003

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
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>>> publications, starting in 2001, for the inventions covered in <<<
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>>> publications. The publication number, patent kind code, and <<<
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>>> enter this cluster. <<<

>>> <<<
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>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.


```

=> s l1
      875 GLP
3460037 1
      466 GLP-1
          (GLP(W)1)
      3994 GLUCAGON
1967462 LIKE
      69438 PEPTIDE
3460037 1
      315 GLUCAGON-LIKE-PEPTIDE-1
          (GLUCAGON(W)LIKE(W)PEPTIDE(W)1)
L4      532 GLP-1 OR GLUCAGON-LIKE-PEPTIDE-1

=> sd his
SD IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d his
      (FILE 'HOME' ENTERED AT 13:20:02 ON 15 MAY 2003)

      FILE 'BIOSIS, MEDLINE, EMBASE, WPIDS, FSTA, JICST-EPLUS' ENTERED AT
      13:20:32 ON 15 MAY 2003
L1      5392 S GLP-1 OR GLUCAGON-LIKE-PEPTIDE-1
L2      619 S L1 AND PH
L3      5 S L2 AND PRESERVATIVE

      FILE 'USPATFULL' ENTERED AT 13:22:18 ON 15 MAY 2003
L4      532 S L1

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1967462 LIKE
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3460037 1
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L5      447 L1 AND PH

=> s l3
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          (GLUCAGON(W)LIKE(W)PEPTIDE(W)1)
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      32083 PRESERVATIVE
L6      83 L2 AND PRESERVATIVE

=> s l3 not l6
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3460037 1

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 3460037 1
 315 GLUCAGON-LIKE-PEPTIDE-1
 (GLUCAGON(W)LIKE(W)PEPTIDE(W)1)
 338034 PH
 32083 PRESERVATIVE
 L7 0 L3 NOT L6

=> s 16 and derivative
 193832 DERIVATIVE
 L8 53 L6 AND DERIVATIVE

=> s 18 and buffer
 324107 BUFFER
 L9 50 L8 AND BUFFER

=> s 19 and TRIS
 105590 TRIS
 L10 35 L9 AND TRIS

=> s 110 and surfactant
 97072 SURFACTANT
 L11 25 L10 AND SURFACTANT

=> s 111 and brij-35
 4192 BRIJ
 1330115 35
 1330 BRIJ-35
 (BRIJ(W)35)
 L12 1 L11 AND BRIJ-35

=> d 112 ti abs ibib tot

L12 ANSWER 1 OF 1 USPATFULL
 TI DERIVATIVES OF GLP-1 ANALOGS
 AB The present invention relates to a pharmaceutical composition comprising
 a GLP-1 derivative having a lipophilic substituent; and a surfactant.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2001:123563 USPATFULL
 TITLE: DERIVATIVES OF GLP-1 ANALOGS
 INVENTOR(S): KNUDSEN, LISELOTTE BJERRE, VALBY, Denmark
 HUUSFELDT, PER OLAF, KOBENHAVN K, Denmark
 NIELSEN, PER FRANKLIN, VARLOSE, Denmark
 KAARSHOLM, NIELS C., VANLOSE, Denmark
 OLSEN, HELLE BIRK, ALLEROD, Denmark
 BJORN, SOREN ERIK, LYNGBY, Denmark
 PEDERSEN, FREDDY ZIMMERDAHL, VARLOSE, Denmark
 MADSEN, KJELD, VARLOSE, Denmark

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001011071	A1	20010802
	US 6458924	B2	20021001
APPLICATION INFO.:	US 1999-398111	A1	19990916 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1999-265141, filed on 8 Mar 1999, PENDING Continuation-in-part of Ser. No. US 1999-258750, filed on 26 Feb 1999, PENDING Continuation-in-part of Ser. No. US 1998-38432, filed on 11 Mar 1998, ABANDONED Continuation-in-part of Ser.		

No. US 1997-918810, filed on 26 Aug 1997, ABANDONED A
371 of International Ser. No. WO 1997-DK340, filed on
22 Aug 1997, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	DK 1996-931	19960830
	DK 1996-1259	19961108
	DK 1996-1470	19961220
	DK 1998-263	19980227
	DK 1998-264	19980227
	DK 1998-268	19980227
	EP 1998-610006	19980313
	DK 1998-507	19980408
	DK 1998-272	19980227
	DK 1998-274	19980227
	DK 1998-508	19980408
	DK 1998-509	19980408
	US 1997-35904P	19970124 (60)
	US 1997-36226P	19970125 (60)
	US 1997-36255P	19970124 (60)
	US 1998-78422P	19980318 (60)
	US 1998-82478P	19980421 (60)
	US 1998-82479P	19980421 (60)
	US 1998-82480P	19980421 (60)
	US 1998-82802P	19980423 (60)
	US 1998-84357P	19980505 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	STEVE T ZELSON, NOVO NORDISK OF NORTH AMERICA INC, 405 LEXINGTON AVENUE, SUITE 6400, NEW YORK, NY, 101746401	
NUMBER OF CLAIMS:	238	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	1 Drawing Page(s)	
LINE COUNT:	15340	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		